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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/990,413	11/21/2001	Nancy Allbritton	Q048	6314

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EXAMINER	
BRUSCA, JOHN S	

ART UNIT	PAPER NUMBER
1631	

DATE MAILED: 09/19/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/990,413	ALLBRITTON ET AL.	
	Examiner	Art Unit	
	John S. Brusca	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 June 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *66-100* is/are pending in the application.

4a) Of the above claim(s) *84 and 85* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *66-70,72,75-83,86,91-93 and 99* is/are rejected.

7)☒ Claim(s) *71-74,87-90,94-98 and 100* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *8/16/2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152).
6) ☐ Other: _____.

SDO

DETAILED ACTION

1. This application has been reassigned to a new examiner.

2. In the amendment filed 06 June 2005 the status identifiers of claims 83-85 were incorrectly listed as Previously presented and should have been listed as Withdrawn. The claims will remain withdrawn and not further addressed in this Office action. In future claim listings the applicants are required to use the correct status identifier for withdrawn claims 83-85.

3. For the purpose of examination, the phrase "introducing reporter molecules into the cell" in claim 66 is interpreted to require that molecules that have the properties of reporter molecules are introduced into the cell, and to not read on a method of introducing a gene that subsequently expresses a reporter molecule into the cell. This is in agreement with the description of reporter molecules on page 20, line 14 to page 21, line 6 in the instant specification.

Continued Examination Under 37 CFR 1.114

4. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 06 June 2005 has been entered.

Specification

5. The abstract of the disclosure is objected to because it is too long. Correction is required. See MPEP § 608.01(b).

6. The amendment to the first sentence of the specification and the Application Data Sheet filed 06 June 2005 has not been entered for the reason detailed below regarding the improper

claim for priority. If a petition under 37 CFR 1.78(a)(3) is made the amendment to the specification or a revised Application Data sheet must accompany the petition.

Priority

7. The benefit claim filed on 06 June 2005 was not entered because the required reference was not timely filed within the time period set forth in 37 CFR 1.78(a)(2) or (a)(5). If the application is an application filed under 35 U.S.C. 111(a) on or after November 29, 2000, the reference to the prior application must be submitted during the pendency of the application and within the later of four months from the actual filing date of the application or sixteen months from the filing date of the prior application. If the application is a nonprovisional application which entered the national stage from an international application filed on or after November 29, 2000, after compliance with 35 U.S.C. 371, the reference to the prior application must be made during the pendency of the application and within the later of four months from the date on which the national stage commenced under 35 U.S.C. 371(b) or (f) or sixteen months from the filing date of the prior application. See 37 CFR 1.78(a)(2)(ii) and (a)(5)(ii). If applicant desires the benefit under 35 U.S.C. 120 based upon a previously filed application, applicant must file a petition for an unintentionally delayed benefit claim under 37 CFR 1.78(a)(3) or (a)(6). The petition must be accompanied by: (1) the reference required by 35 U.S.C. 120 or 119(e) and 37 CFR 1.78(a)(2) or (a)(5) to the prior application (unless previously submitted); (2) a surcharge under 37 CFR 1.17(t); and (3) a statement that the entire delay between the date the claim was due under 37 CFR 1.78(a)(2) or (a)(5) and the date the claim was filed was unintentional. The Director may require additional information where there is a question whether the delay was

unintentional. The petition should be addressed to: Mail Stop Petition, Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450.

8. It is noted that the claim to U.S. Provisional Application No. 60/252861 is improper because the provisional application does not also claim priority to U.S. Application Nos. 09/358504 and 09/036706 (see MPEP 201.11). Amendments in the claimed parent provisional application is required to claim the chain of applications the applicants have attempted to claim in the Application Data Sheet filed 06 June 2005. The applicants have attempted to correct what appears to be a typographical error in the instant application claim for priority by amending the claimed parent application number from 09/358505 to 09/358504. The same apparent error exists in U.S. Provisional Application No. 60/252861.

9. For the purpose of examination, the instant application is given the benefit of priority only to the filing date of U.S. Provisional Application No. 60/252861, filed on 22 November 2000, until such time that the claim for priority to U.S. Applications 09/358504 and 09/036706 are perfected.

Claim Rejections - 35 USC § 112

10. The rejection of claims 66-82 and 86-101 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention in the Office action mailed 03 June 2004 is withdrawn in view of the arguments and amendments filed 06 June 2005.

11. The rejection of claims 66-82 and 86-101 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement in the Office action mailed 03 June 2004 is withdrawn in view of the arguments and amendments filed 06 June 2005.

Claim Rejections - 35 USC § 102

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

13. Claims 66, 67, 75, 76, 78, 79, 82, 86, 91, 92, 93, and 99 are rejected under 35 U.S.C. 102(b) as being anticipated by Lee et al.

The claims are drawn to a method of insertion of a plurality of enzyme substrates to a cell, and subsequently isolating and analyzing the processed substrates by electrophoresis. In some embodiments the substrates comprise fluorescent labels, the reaction in the cell is stopped within a second, three substrate-enzyme combinations are assayed simultaneously, and the substrates are present at less than 1 micromolar.

Lee et al. shows on page 761 and figure 6 the analysis of three fluorescently labeled protein kinase substrates. The substrates were introduced into a single cell, and subsequently removed and isolated from cellular components (thereby stopping the processing of the substrates) in a time frame of 350 milliseconds (see the description of the sampling procedure on the second column of page 760. The processed substrates are analyzed by capillary electrophoresis. Lee et al. shows detection limits of their procedure in figure 5 of final concentration after dilution in an oocyte of as little as 20 nanomolar. Lee et al. shows introduction of substrates to cells at initial concentration of as little as 0.5 micromolar

Claim Rejections - 35 USC § 103

14. The rejection of claims 66-82 and 86-101 under 35 U.S.C. 103(a) as being unpatentable over Day et al. (1998) taken with Sims et al. (1998) in view of Wright (US 5,639,656 A) in the Office action mailed 03 June 2004 is withdrawn in view of the arguments and amendments filed 06 June 2005.

15. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

16. The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

17. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

18. Claims 66, 68-70, and 72 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lee et al.

The claims are drawn to a method of insertion of a plurality of enzyme substrates to a cell, and subsequently isolating and analyzing the processed substrates, followed by recording the results. In some embodiments the cells are exposed to compound.

Lee et al. shows on page 761 and figure 6 the analysis of three fluorescently labeled protein kinase substrates. The substrates were introduced into a single cell, and subsequently removed and isolated from cellular components. Lee et al. shows treatment of cells with a single substrate with PMA or LPA in figure 4 to measure the effects of these compounds on phosphorylation of the substrate. Lee et al. shows the results of the time course of stimulation of phosphorylation of the substrate by the two compounds in figures 4D and 4E. Lee et al. does not show external stimulus of cells which comprise a plurality of enzyme substrates. Lee et al. does not show explicit tabulation of results or generation of a map of responses to the two compounds.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to stimulate cells comprising a plurality of enzyme substrates with a compound because Lee et al. shows that their method may be used to analyze processing of enzyme substrates and that their method may be used to determine the effect of a compound on processing of a substrate, for the purpose of determining the effect of a compound on the activity of a plurality of cellular enzymes simultaneously. It would have been further obvious to tabulate the results of such experiments in the format of figure 4D and 4E or in other formats so that the results could be recorded for future reference and comparison to other assays.

Double Patenting

19. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

20. An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim is not patentably distinct from the reference claim(s) because the examined claim is either anticipated by, or would be obvious over, the reference claim(s). see, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985).

21. Claims 66, 67, 69, 70, 75-77, 82, and 83 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 3, 4, 6, 9, and 12 of U.S. Patent No. 6,335,201. Although the conflicting claims are not identical, they are not patentably distinct from each other because the differences between the instant claims and the cited claims of U.S, Patent No. 6,335,201 are minor in nature.

22. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(f) he did not himself invent the subject matter sought to be patented.

23. Claims 66, 67, 69, 70, 75-77, 82, and 83 rejected under 35 U.S.C. 102(f) because the applicant did not invent the claimed subject matter.

For the reasons discussed above, it is apparent that U.S. Patent No. 6,335,201 contains claimed subject matter in claims that is not patentably distinct from instant claims 66, 67, 69, 70, 75-77, 82, and 83. Because the inventive entity of U.S. Patent No. 6,335,201 is different from the instant application, a rejection is appropriate under 35 U.S.C. 102(f). This rejection could be overcome by amendment of the appropriate claims so that the claims are patentably distinct, or by filing a declaration stating the inventive entity for the commonly claimed subject matter is identical.

24. Claims 68-70, 75, 76, and 82 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 2, 4, 5, 7, and 17 of U.S. Patent No. 6,740,497 Although the conflicting claims are not identical, they are not patentably

distinct from each other because the claims of U.S. Patent No. 6,740,497 are drawn to oncoprotein species of substrate target.

25. Claims 66, 67, and 80-82 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 48, 50, 51, 59, and 70 of copending Application No. 09/945396. Although the conflicting claims are not identical, they are not patentably distinct from each other because copending Application No. 09/945396 claims a method which uses a laser generated shock wave species of isolation relative to the instant generic releasing and detection steps.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

26. Claims 66, 67, and 80-82 are rejected under 35 U.S.C. 102(f) because the applicant did not invent the claimed subject matter.

For the reasons discussed above, it is apparent that copending Application No. 09/945396 contains claimed subject matter in claims that is not patentably distinct from instant claims 66, 67, and 80-82. Because the inventive entity of copending Application 09/945396 is different from the instant application, a rejection is appropriate under 35 U.S.C. 102(f). This rejection could be overcome by amendment of the appropriate claims so that the claims are patentably distinct, or by filing a declaration stating the inventive entity for the commonly claimed subject matter is identical.

27. Claims 66, 67, 69, and 70 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 54, 56, 58, 62, and 63 of Application No. 10/779917 Although the conflicting claims are not identical, they are not

patentably distinct from each other because the claims of Application No. 10/779917 are drawn to oncoprotein species of substrate target.

Allowable Subject Matter

28. Claims 71, 73, 74, 87-90, 94-98, and 100 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Conclusion

29. Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center at (800) 786-9199.Any inquiry concerning this communication or earlier communications from the examiner

should be directed to John S. Brusca whose telephone number is 571 272-0714. The examiner can normally be reached on M-F 8:30 AM - 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel, PhD. can be reached on 571 272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

John S. Brusca 12 September 2005

John S. Brusca
Primary Examiner
Art Unit 1631

jsb